

What is claimed is:

1. An isolated nucleic acid encoding a mammalian NPFF receptor.
2. The nucleic acid of claim 1, wherein the nucleic acid is DNA.
3. The DNA of claim 2, wherein the DNA is cDNA.
4. The DNA of claim 2, wherein the DNA is genomic DNA.
5. The nucleic acid of claim 1, wherein the nucleic acid is RNA.
6. The nucleic acid of claim 1, wherein the mammalian NPFF receptor is a NPFF1 receptor.
7. The nucleic acid of claim 6, wherein the mammalian NPFF1 receptor is a rat NPFF1 receptor.
8. The nucleic acid of claim 6, wherein the mammalian NPFF1 receptor is a human NPFF1 receptor.
9. The nucleic acid of claim 1, wherein the mammalian NPFF receptor is a NPFF2 receptor.
10. The nucleic acid of claim 9, wherein the mammalian NPFF2 receptor is a human NPFF2 receptor.
11. The nucleic acid of claim 7, wherein the rat NPFF1 receptor has an amino acid sequence identical to that encoded by the plasmid pEXJ-rNPFF1 (ATCC Accession No. 203184).

12. The nucleic acid of claim 7, wherein the rat NPFF1 receptor has an amino acid sequence identical to the amino acid sequence shown in Figure 2 (Seq. I.D. No. 2).
13. The nucleic acid of claim 8, wherein the human NPFF1 receptor has an amino acid sequence identical to that encoded by plasmid pWE15-hNPFF1 (ATCC Accession No. 203183).
14. The nucleic acid of claim 8, wherein the human NPFF1 receptor has an amino acid sequence identical to the amino acid sequence shown in Figure 5 (Seq. I.D. No. 4).
15. The nucleic acid of claim 8, wherein the human NPFF1 receptor has an amino acid sequence identical to that encoded by plasmid pCDNA3.1-hNPFF1 (ATCC Accession No. 203605).
16. The nucleic acid of claim 8, wherein the human NPFF1 receptor has an amino acid sequence identical to the amino acid sequence shown in Figure 12 (Seq. I.D. No. 8).
17. The nucleic acid of claim 10, wherein the human NPFF2 receptor has an amino acid sequence identical to that encoded by plasmid pCDNA3.1-hNPFF2b (ATCC Accession No. 203255).
18. The nucleic acid of claim 10, wherein the human NPFF2 receptor has an amino acid sequence identical to the amino acid sequence shown in Figure 8 (Seq. I.D. No. 6).

19. The nucleic acid of claim 1, wherein the nucleic acid
(a) hybridizes to a nucleic acid having the defined
sequence shown in Figure 1 (Seq. I.D. No. 1) under
low stringency conditions or a sequence complementary
thereto and (b) is further characterized by its
ability to cause a change in the pH of a culture of
CHO cells when a NPFF peptide is added to the culture
and the CHO cells express the nucleic acid which
hybridized to the nucleic acid having the defined
sequence of its complement.
20. The nucleic acid of claim 1, wherein the nucleic acid
(a) hybridizes to a nucleic acid having the defined
sequence shown in Figure 4 (Seq. I.D. No. 3) under
low stringency conditions or a sequence complementary
thereto and (b) is further characterized by its
ability to cause a change in the pH of a culture of
CHO cells when a NPFF peptide is added to the culture
and the CHO cells express the nucleic acid which
hybridized to the nucleic acid having the defined
sequence or its complement.
21. The nucleic acid of claim 1, wherein the nucleic acid
(a) hybridizes to a nucleic acid having the defined
sequence shown in Figure 7 (Seq. ID No. 5) under low
stringency conditions or a sequence complementary
thereto and (b) is further characterized by its
ability to cause a change in the pH of a culture of
CHO cells when a NPFF peptide is added to the culture
and the CHO cells express the nucleic acid which
hybridized to the nucleic acid having the defined
sequence or its complement.

22. The nucleic acid of claim 1, wherein the nucleic acid
(a) hybridizes to a nucleic acid having the defined
sequence shown in Figure 11 (Seq. I.D. No. 7) under
low stringency conditions or a sequence complementary
thereto and (b) is further characterized by its
ability to cause a change in the pH of a culture of
CHO cells when a NPFF peptide is added to the culture
and the CHO cells express the nucleic acid which
hybridized to the nucleic acid having the defined
sequence or its complement.
23. A purified mammalian NPFF receptor protein.
24. The purified mammalian NPFF receptor protein of claim
23, wherein the NPFF receptor protein is a NPFF1
receptor protein.
25. The purified mammalian NPFF receptor protein of claim
23, wherein the NPFF receptor protein is a NPFF2
receptor protein.
26. The purified mammalian NPFF1 receptor protein of
claim 24, wherein the NPFF1 receptor protein is a rat
NPFF1 receptor protein.
27. The purified mammalian NPFF1 receptor protein of
claim 24, wherein the NPFF1 receptor protein is a
human NPFF1 receptor protein.
28. The purified mammalian NPFF2 receptor protein of
claim 25, wherein the NPFF2 receptor protein is a
human NPFF2 receptor protein.
29. A vector comprising the nucleic acid of claim 1.

30. A vector comprising the nucleic acid of claim 6.
31. A vector comprising the nucleic acid of claim 9.
- 5 32. A vector comprising the nucleic acid of any of claims 19, 20, 21, or 22.
- 10 33. A vector of any of claims 19, 20, 21, 22, 29, 30, or 31 adapted for expression in a cell which comprises the regulatory elements necessary for expression of the nucleic acid in the cell operatively linked to the nucleic acid encoding the receptor so as to permit expression thereof, wherein the cell is a bacterial, amphibian, yeast, insect or mammalian cell.
- 15 34. The vector of claim 33, wherein the vector is a baculovirus.
- 20 35. The vector of claim 29, wherein the vector is a plasmid.
- 25 36. The plasmid of claim 35 designated pEXJ-rNPFF1 (ATCC Accession No. 203184).
37. The plasmid of claim 35 designated pWE15-hNPFF1 (ATCC Accession No. 203183).
- 30 38. The plasmid of claim 35 designated pCDNA3.1-hNPFF2b (ATCC Accession No. 203255).
39. The plasmid of claim 35 designated pCDNA3.1-hNPFF1 (ATCC Accession No. 203605).

40. A cell comprising the vector of claim 33.

41. A cell of claim 40, wherein the cell is a non-mammalian cell.

42. A cell of claim 41, wherein the non-mammalian cell is a *Xenopus* oocyte cell or a *Xenopus* melanophore cell.

43. A cell of claim 40, wherein the cell is a mammalian cell.

44. A mammalian cell of claim 43, wherein the cell is a COS-7 cell, a 293 human embryonic kidney cell, a NIH-3T3 cell, a LM(tk-) cell, a mouse Y1 cell, or a CHO cell.

45. An insect cell comprising the vector of claim 33.

46. An insect cell of claim 45, wherein the insect cell is an Sf9 cell, an Sf21 cell or a *Trichoplusia ni* 5B1-4 cell.

47. A membrane preparation isolated from the cell of any of claims 40, 41, 43, 44, 45 or 46.

48. A nucleic acid probe comprising at least 15 nucleotides, which probe specifically hybridizes with a nucleic acid encoding a mammalian NPFF receptor, wherein the probe has a unique sequence corresponding to a sequence present within one of the two strands of the nucleic acid encoding the mammalian NPFF1 receptor and contained in plasmid pEXJ-rNPFF1 (ATCC Accession No. 203184), plasmid pWE15-hNPFF1 (ATCC Accession No. 203183), plasmid pCDNA3.1-hNPFF2b (ATCC

-139-

Accession No. 203255), or plasmid p
Accession No. 203605).

nucleic acid probe comprising
otides, which probe specifically h
leic acid encoding a mammalian
in the probe has a unique sequence
sequence present within (a) the
nce shown in Figure 1 (Seq. I.D.
reverse complement thereto.

nucleic acid probe comprising
otides, which probe specifically h
leic acid encoding a mammalian
in the probe has a unique sequence
sequence present within (a) the
nce shown in Figure 4 (Seq. I.D.
reverse complement thereto.

nucleic acid probe comprising
otides, which probe specifically h
leic acid encoding a mammalian
in the probe has a unique sequence
sequence present within (a) th
nce shown in Figure 7 (Seq. I.D.
reverse complement thereto.

nucleic acid probe comprising
otides, which probe specifically
leic acid encoding a mammalian
in the probe has a unique sequence
sequence present within (a) th
nce shown in Figure 11 (Seq. I.D.
reverse complement thereto.

49. A nucleic acid probe comprising at least 15 nucleotides, which probe specifically hybridizes with a nucleic acid encoding a mammalian NPFF receptor, wherein the probe has a unique sequence corresponding to a sequence present within (a) the nucleic acid sequence shown in Figure 1 (Seq. I.D. No. 1) or (b) the reverse complement thereto.
50. A nucleic acid probe comprising at least 15 nucleotides, which probe specifically hybridizes with a nucleic acid encoding a mammalian NPFF receptor, wherein the probe has a unique sequence corresponding to a sequence present within (a) the nucleic acid sequence shown in Figure 4 (Seq. I.D. No. 3) or (b) the reverse complement thereto.
51. A nucleic acid probe comprising at least 15 nucleotides, which probe specifically hybridizes with a nucleic acid encoding a mammalian NPFF receptor, wherein the probe has a unique sequence corresponding to a sequence present within (a) the nucleic acid sequence shown in Figure 7 (Seq. I.D. No. 5) or (b) the reverse complement thereto.
52. A nucleic acid probe comprising at least 15 nucleotides, which probe specifically hybridizes with a nucleic acid encoding a mammalian NPFF receptor, wherein the probe has a unique sequence corresponding to a sequence present within (a) the nucleic acid sequence shown in Figure 11 (Seq. I.D. No. 7) or (b) the reverse complement thereto.

53. The nucleic acid probe of claim 49, 50, 51, or 52,
wherein the nucleic acid is DNA.
- 5 54. The nucleic acid probe of claim 49, 50, 51, or 52,
wherein the nucleic acid is RNA.
- 10 55. An antisense oligonucleotide having a sequence
capable of specifically hybridizing to the RNA of
claim 5, so as to prevent translation of the RNA.
- 15 56. An antisense oligonucleotide having a sequence
capable of specifically hybridizing to the genomic
DNA of claim 4, so as to prevent transcription of the
genomic DNA.
- 20 57. An antisense oligonucleotide of claim 55 or 56,
wherein the oligonucleotide comprises chemically
modified nucleotides or nucleotide analogues.
- 25 58. An antibody capable of binding to a mammalian NPFF
receptor encoded by the nucleic acid of claim 1.
59. An antibody of claim 58, wherein the mammalian NPFF
receptor is a human NPFF1 receptor.
60. An antibody of claim 58, wherein the mammalian NPFF
receptor is a rat NPFF1 receptor.
- 30 61. An antibody of claim 58, wherein the mammalian NPFF
receptor is a human NPFF2 receptor.
62. An agent capable of competitively inhibiting the
binding of the antibody of claim 58 to a mammalian

NPFF receptor.

63. An antibody of claim 58, wherein the antibody is a monoclonal antibody or antisera.
- 5
64. A pharmaceutical composition comprising (a) an amount of the oligonucleotide of claim 55 capable of passing through a cell membrane and effective to reduce expression of a mammalian NPFF receptor and (b) a pharmaceutically acceptable carrier capable of passing through the cell membrane.
- 10
65. A pharmaceutical composition of claim 64, wherein the oligonucleotide is coupled to a substance which inactivates mRNA.
- 15
66. A pharmaceutical composition of claim 65, wherein the substance which inactivates mRNA is a ribozyme.
- 20
67. A pharmaceutical composition of claim 65, wherein the pharmaceutically acceptable carrier comprises a structure which binds to a mammalian NPFF receptor on a cell capable of being taken up by the cells after binding to the structure.
- 25
68. A pharmaceutical composition of claim 67, wherein the pharmaceutically acceptable carrier is capable of binding to a mammalian NPFF receptor which is specific for a selected cell type.
- 30
69. A pharmaceutical composition which comprises an amount of the antibody of claim 58 effective to block binding of a ligand to a human NPFF receptor and a pharmaceutically acceptable carrier.

70. A transgenic, nonhuman mammal expressing DNA encoding a mammalian NPFF receptor of claim 1.
- 5 71. A transgenic, nonhuman mammal comprising a homologous recombination knockout of the native mammalian NPFF receptor.
- 10 72. A transgenic, nonhuman mammal whose genome comprises antisense DNA complementary to the DNA encoding a mammalian NPFF receptor of claim 1 so placed within the genome as to be transcribed into antisense mRNA which is complementary to mRNA encoding the mammalian NPFF receptor and which hybridizes to mRNA encoding the mammalian NPFF receptor, thereby reducing its translation.
- 15 73. The transgenic, nonhuman mammal of claim 70 or 71, wherein the DNA encoding the mammalian NPFF receptor additionally comprises an inducible promoter.
- 20 74. The transgenic, nonhuman mammal of claim 70 or 71, wherein the DNA encoding the mammalian NPFF receptor additionally comprises tissue specific regulatory elements.
- 25 75. A transgenic, nonhuman mammal of claim 70, 71, or 72, wherein the transgenic, nonhuman mammal is a mouse.
- 30 76. A process for identifying a chemical compound which specifically binds to a mammalian NPFF receptor which comprises contacting cells containing DNA encoding and expressing on their cell surface the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, with the

compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the mammalian NPFF receptor.

- 5 77. A process for identifying a chemical compound which specifically binds to a mammalian NPFF receptor which comprises contacting a membrane preparation from cells containing DNA encoding and expressing on their cell surface the mammalian NPFF receptor, wherein
10 such cells do not normally express the mammalian NPFF receptor, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the mammalian NPFF receptor. ✓
- 15 78. The process of claim 76 or 77, wherein the mammalian NPFF receptor is a human NPFF1 receptor.
79. The process of claim 76 or 77, wherein the mammalian NPFF receptor is a human NPFF2 receptor.
- 20 80. The process of claim 76 or 77, wherein the mammalian NPFF receptor has substantially the same amino acid sequence as the human NPFF1 receptor encoded by plasmid pWE15-hNPFF1 (ATCC Accession No. 203183).
- 25 81. The process of claim 76 or 77, wherein the mammalian NPFF receptor has substantially the same amino acid sequence as the human NPFF1 receptor encoded by plasmid pCDNA3.1-hNPFF1 (ATCC Accession No. 203605).
- 30 82. The process of claim 65 or 66, wherein the mammalian NPFF receptor has substantially the same amino acid sequence as the human NPFF2 receptor encoded by plasmid pCDNA3.1-hNPFF2b (ATCC Accession No. 203255).

83. The process of claim 76 or 77, wherein the mammalian NPFF receptor has substantially the same amino acid sequence as that shown in Figure 5 (Seq. I.D. No. 4).
- 5 84. The process of claim 76 or 77, wherein the mammalian NPFF receptor has the amino acid sequence shown in Figure 5 (Seq. I.D. No. 4).
- 10 85. The process of claim 76 or 77, wherein the mammalian NPFF receptor has substantially the same amino acid sequence as that shown in Figure 8 (Seq. I.D. No. 6).
- 15 86. The process of claim 76 or 77, wherein the mammalian NPFF receptor has the same amino acid sequence shown in Figure 8 (Seq. I.D. No. 6).
- 20 87. The process of claim 76 or 77, wherein the mammalian NPFF receptor has substantially the same amino acid sequence as that shown in Figure 12 (Seq. I.D. No. 8).
- 25 88. The process of claim 76 or 77, wherein the mammalian NPFF receptor has the same amino acid sequence shown in Figure 12 (Seq. I.D. No. 8).
- 30 89. The process of claim 76 or 77, wherein the compound is not previously known to bind to a mammalian NPFF receptor.
90. A compound identified by the process of claim 89.
91. A process of claim 76 or 77, wherein the cell is an insect cell.

92. The process of claim 76 or 77, wherein the cell is a mammalian cell.

93. The process of claim 92, wherein the cell is nonneuronal in origin.

94. The process of claim 93, wherein the nonneuronal cell is a COS-7 cell, a human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.

95. A process of claim 92, wherein the compound is a compound not previously known to bind to a mammalian NPFF receptor.

96. A compound identified by the process of claim 95.

97. A process involving competitive binding for identifying a chemical compound which specifically binds to a mammalian NPFF receptor which comprises separately contacting cells expressing on their cell surface the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting specific binding of the chemical compound to the mammalian NPFF receptor, a decrease in the binding of the second chemical compound to the mammalian NPFF receptor in the presence of the chemical compound indicating that the chemical compound binds to the mammalian NPFF receptor.

98. A process involving competitive binding for identifying a chemical compound which specifically binds to a mammalian NPFF receptor which comprises separately contacting a membrane preparation from cells expressing on their cell surface the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting specific binding of the chemical compound to the mammalian NPFF receptor, a decrease in the binding of the second chemical compound to the mammalian NPFF receptor in the presence of the chemical compound indicating that the chemical compound binds to the mammalian NPFF receptor.
99. A process of claim 97 or 98, wherein the mammalian NPFF receptor is a human NPFF1 receptor.
100. A process of claim 97 or 98, wherein the mammalian NPFF receptor is a human NPFF2 receptor.
101. The process of claim 97 or 98, wherein the cell is an insect cell.
102. The process of claim 97 or 98, wherein the cell is a mammalian cell.
103. The process of claim 102, wherein the cell is nonneuronal in origin.

104. The process of claim 103, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.

105. The process of claim 104, wherein the compound is not previously known to bind to a mammalian NPFF receptor.

106. A compound identified by the process of claim 105.

107. A method of screening a plurality of chemical compounds not known to bind to a mammalian NPFF receptor to identify a compound which specifically binds to the mammalian NPFF receptor, which comprises

(a) contacting cells transfected with and expressing DNA encoding the mammalian NPFF receptor with a compound known to bind specifically to the mammalian NPFF receptor;

(b) contacting the preparation of step (a) with the plurality of compounds not known to bind specifically to the mammalian NPFF receptor, under conditions permitting binding of compounds known to bind to the mammalian NPFF receptor;

(c) determining whether the binding of the compound known to bind to the mammalian NPFF receptor is reduced in the presence of any compound within the plurality of compounds.

relative to the binding of the compound in the absence of the plurality of compounds; and if so

- 5 (d) separately determining the binding to the mammalian NPFF receptor of compounds included in the plurality of compounds, so as to thereby identify the compound which specifically binds to the mammalian NPFF
10 receptor.

108. A method of screening a plurality of chemical compounds not known to bind to a mammalian NPFF receptor to identify a compound which
15 specifically binds to the mammalian NPFF receptor, which comprises

- (a) contacting a membrane preparation from cells transfected with and expressing DNA encoding the mammalian NPFF receptor with the
20 plurality of compounds not known to bind specifically to the mammalian NPFF receptor under conditions permitting binding of compounds known to bind to the mammalian NPFF receptor;
25

- (b) determining whether the binding of a compound known to bind to the mammalian NPFF receptor is reduced in the presence of any
30 compound within the plurality of compounds, relative to the binding of the compound in the absence of the plurality of compounds; and if so

- (c) separately determining the binding to the mammalian NPFF receptor of compounds included in the plurality of compounds, so as to thereby identify the compound which specifically binds to the mammalian NPFF receptor.

109. A method of claim 107 or 108, wherein the mammalian NPFF receptor is a human NPFF1 receptor.

110. A method of claim 107 or 108, wherein the mammalian NPFF receptor is a human NPFF2 receptor.

111. A method of claim 107, 108, 109, or 110, wherein the cell is a mammalian cell.

112. A method of claim 111, wherein the mammalian cell is non-neuronal in origin.

113. The method of claim 112, wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a LM(tk-) cell, a CHO cell, a mouse Y1 cell, or an NIH-3T3 cell.

114. A method of detecting expression of a mammalian NPFF receptor by detecting the presence of mRNA coding for the mammalian NPFF receptor which comprises obtaining total mRNA from the cell and contacting the mRNA so obtained with the nucleic acid probe of any of claims 48, 49, 50, 51, or 52 under hybridizing conditions, detecting the presence of mRNA hybridizing to the probe, and

thereby detecting the expression of the mNPFF receptor by the cell.

A method of detecting the presence of a mNPFF receptor on the surface of a cell comprises contacting the cell with the of claim 58 under conditions permitting of the antibody to the receptor, detecting presence of the antibody bound to the cell thereby detecting the presence of the mNPFF receptor on the surface of the cell.

A method of determining the physiological of varying levels of activity of mammalian receptors which comprises producing a transgenic nonhuman mammal of claim 73 whose mammalian NPFF receptor activity are varied by use of an inducible promoter which regulates mammalian NPFF receptor expression.

A method of determining the physiological of varying levels of activity of mammalian receptors which comprises producing a transgenic, nonhuman mammals of claim 73 expressing a different amount of mammalian NPFF receptor.

A method for identifying an antagonist capable of alleviating an abnormality, where the abnormality is alleviated by decreasing activity of a mammalian NPFF receptor, comprising administering a compound to the transgenic nonhuman mammal of claim 70, 73, 74, or 75 and determining whether the compound alleviates the abnormality.

- 5 115. A method of detecting the presence of a mammalian NPFF receptor on the surface of a cell which comprises contacting the cell with the antibody of claim 58 under conditions permitting binding of the antibody to the receptor, detecting the presence of the antibody bound to the cell, and thereby detecting the presence of the mammalian NPFF receptor on the surface of the cell.
- 10
- 15 116. A method of determining the physiological effects of varying levels of activity of mammalian NPFF receptors which comprises producing a transgenic, nonhuman mammal of claim 73 whose levels of mammalian NPFF receptor activity are varied by use of an inducible promoter which regulates mammalian NPFF receptor expression.
- 20
- 25 117. A method of determining the physiological effects of varying levels of activity of mammalian NPFF receptors which comprises producing a panel of transgenic, nonhuman mammals of claim 73 each expressing a different amount of mammalian NPFF receptor.
- 30 118. A method for identifying an antagonist capable of alleviating an abnormality wherein the abnormality is alleviated by decreasing the activity of a mammalian NPFF receptor comprising administering a compound to the transgenic, nonhuman mammal of claim 70, 73, 74, or 75, and determining whether the compound alleviates the

physical and behavioral abnormalities displayed by the transgenic, nonhuman mammal as a result of overactivity of a mammalian NPFF receptor, the alleviation of the abnormality identifying the compound as an antagonist.

119. The method of claim 118, wherein the mammalian NPFF receptor is a human NPFF1 receptor.

120. The method of claim 118, wherein the mammalian NPFF receptor is a human NPFF2 receptor.

121. An antagonist identified by the method of claim 118.

122. A pharmaceutical composition comprising an antagonist of claim 121 and a pharmaceutically acceptable carrier.

123. A method of treating an abnormality in a subject wherein the abnormality is alleviated by decreasing the activity of a mammalian NPFF receptor which comprises administering to the subject an effective amount of the pharmaceutical composition of claim 122, thereby treating the abnormality.

124. A method for identifying an agonist capable of alleviating an abnormality in a subject wherein the abnormality is alleviated by increasing the activity of a mammalian NPFF receptor comprising administering a compound to the transgenic, nonhuman mammal of claim 70, 73, 74, or 75, and determining whether the compound alleviates the

physical and behavioral abnormalities displayed by the transgenic, nonhuman mammal, the alleviation of the abnormality identifying the compound as an agonist.

5

125. The method of claim 124, wherein the mammalian NPFF receptor is a human NPFF1 receptor.

10

126. The method of claim 124, wherein the mammalian NPFF receptor is a human NPFF2 receptor.

127. An agonist identified by the method of claim 124.

15

128. A pharmaceutical composition comprising an agonist identified by the method of claim 127 and a pharmaceutically acceptable carrier.

20

129. A method of treating an abnormality in a subject wherein the abnormality is alleviated by increasing the activity of a mammalian NPFF receptor which comprises administering to the subject an effective amount of the pharmaceutical composition of claim 128, thereby treating the abnormality.

25

130. A method for diagnosing a predisposition to a disorder associated with the activity of a specific mammalian allele which comprises:

30

(a) obtaining DNA of subjects suffering from the disorder;

(b) performing a restriction digest of the DNA with a panel of restriction enzymes;

- 5
- 10
- 15
- 20
- 25
- (c) electrophoretically separating the resulting DNA fragments on a sizing gel;
 - (d) contacting the resulting gel with a nucleic acid probe capable of specifically hybridizing with a unique sequence included within the sequence of a nucleic acid molecule encoding a mammalian NPFF receptor and labeled with a detectable marker;
 - (e) detecting labeled bands which have hybridized to the DNA encoding a mammalian NPFF1 receptor of claim 1 labeled with a detectable marker to create a unique band pattern specific to the DNA of subjects suffering from the disorder;
 - (f) preparing DNA obtained for diagnosis by steps (a)-(e); and
 - (g) comparing the unique band pattern specific to the DNA of subjects suffering from the disorder from step (e) and the DNA obtained for diagnosis from step (f) to determine whether the patterns are the same or different and to diagnose thereby predisposition to the disorder if the patterns are the same.

30 131. The method of claim 130, wherein a disorder associated with the activity of a specific mammalian allele is diagnosed.

132. A method of preparing the purified mammalian NPFF

receptor of claim 23 which comprises:

- (a) culturing cells which express the mammalian NPFF receptor;
- (b) recovering the mammalian NPFF receptor from the cells; and
- (c) purifying the mammalian NPFF receptor so recovered.

133. A method of preparing the purified mammalian NPFF receptor of claim 23 which comprises:

- (a) inserting a nucleic acid encoding the mammalian NPFF receptor into a suitable vector;
- (b) introducing the resulting vector into a suitable host cell;
- (c) placing the resulting cell in suitable condition permitting the production of the mammalian NPFF receptor;
- (d) recovering the mammalian NPFF receptor produced by the resulting cell; and
- (e) isolating and/or purifying the mammalian NPFF receptor so recovered.

134. A process for determining whether a chemical compound is a mammalian NPFF receptor agonist which comprises contacting cells transfected with

and expressing DNA encoding the mammalian NPFF receptor with the compound under conditions permitting the activation of the mammalian NPFF receptor, and detecting an increase in mammalian NPFF receptor activity, so as to thereby determine whether the compound is a mammalian NPFF receptor agonist.

135. A process for determining whether a chemical compound is a mammalian NPFF receptor antagonist which comprises contacting cells transfected with and expressing DNA encoding the mammalian NPFF receptor with the compound in the presence of a known mammalian NPFF receptor agonist, under conditions permitting the activation of the mammalian NPFF receptor, and detecting a decrease in mammalian NPFF receptor activity, so as to thereby determine whether the compound is a mammalian NPFF receptor antagonist.

136. A process of claim 134 or 135, wherein the mammalian NPFF receptor is a human NPFF1 receptor.

137. A process of claim 134 or 135, wherein the mammalian NPFF receptor is a human NPFF2 receptor.

138. A pharmaceutical composition which comprises an amount of a mammalian NPFF receptor agonist determined by the process of claim 134 effective to increase activity of a mammalian NPFF receptor and a pharmaceutically acceptable carrier.

139. A pharmaceutical composition of claim 138, wherein the mammalian NPFF receptor agonist is not previously known.

5 140. A pharmaceutical composition which comprises an amount of a mammalian NPFF receptor antagonist determined by the process of claim 135 effective to reduce activity of a mammalian NPFF receptor and a pharmaceutically acceptable carrier.

10 141. A pharmaceutical composition of claim 140, wherein the mammalian NPFF receptor antagonist is not previously known.

15 142. A process for determining whether a chemical compound specifically binds to and activates a mammalian NPFF receptor, which comprises contacting cells producing a second messenger response and expressing on their cell surface the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, with the chemical compound under conditions
20 suitable for activation of the mammalian NPFF receptor, and measuring the second messenger response in the presence and in the absence of the chemical compound, a change in the second messenger response in the presence of the chemical compound indicating that the compound
25 activates the mammalian NPFF receptor.

30 143. The process of claim 142, wherein the second messenger response comprises chloride channel activation and the change in second messenger is an increase in the level of inward chloride

current.

144. A process for determining whether a chemical
compound specifically binds to and inhibits
activation of a mammalian NPFF receptor, which
comprises separately contacting cells producing a
second messenger response and expressing on their
cell surface the mammalian NPFF receptor, wherein
such cells do not normally express the mammalian
NPFF receptor, with both the chemical compound
and a second chemical compound known to activate
the mammalian NPFF receptor, and with only the
second chemical compound, under conditions
suitable for activation of the mammalian NPFF
receptor, and measuring the second messenger
response in the presence of only the second
chemical compound and in the presence of both the
second chemical compound and the chemical
compound, a smaller change in the second
messenger response in the presence of both the
chemical compound and the second chemical
compound than in the presence of only the second
chemical compound indicating that the chemical
compound inhibits activation of the mammalian
NPFF receptor.

145. The process of claim 144, wherein the second
messenger response comprises chloride channel
activation and the change in second messenger
response is a smaller increase in the level of
inward chloride current in the presence of both
the chemical compound and the second chemical
compound than in the presence of only the second
chemical compound.

146. A process of any of claims 142, 143, 144, or 145, wherein the mammalian NPFF receptor is a human NPFF1 receptor.
- 5 147. A process of any of claims 142, 143, 144, or 145, wherein the mammalian NPFF receptor is a human NPFF2 receptor.
- 10 148. The process of any of claims 142, 143, 144, 145, 146, or 147 wherein the cell is an insect cell.
- 15 149. The process of any of claims 142, 143, 144, 145, 146, or 147, wherein the cell is a mammalian cell.
- 20 150. The process of claim 149, wherein the mammalian cell is nonneuronal in origin.
- 25 151. The process of claim 150, wherein the nonneuronal cell is a COS-7 cell, CHO cell, 293 human embryonic kidney cell, NIH-3T3 cell or LM(tk-) cell.
- 30 152. The process of claim 142, 143, 144, or 145, wherein the compound is not previously known to bind to a mammalian NPFF receptor.
153. A compound determined by the process of claim 152.
154. A pharmaceutical composition which comprises an amount of a mammalian NPFF receptor agonist determined by the process of claim 142 or 143 effective to increase activity of a mammalian

NPFF receptor and a pharmaceutically acceptable carrier.

5 155. A pharmaceutical composition of claim 154, wherein the mammalian NPFF receptor agonist is not previously known.

10 156. A pharmaceutical composition which comprises an amount of a mammalian NPFF receptor antagonist determined by the process of claim 144 or 145 effective to reduce activity of a mammalian NPFF receptor and a pharmaceutically acceptable carrier.

15 157. A pharmaceutical composition of claim 156, wherein the mammalian NPFF receptor antagonist is not previously known.

20 158. A method of screening a plurality of chemical compounds not known to activate a mammalian NPFF receptor to identify a compound which activates the mammalian NPFF receptor which comprises:

25 (a) contacting cells transfected with and expressing the mammalian NPFF receptor with the plurality of compounds not known to activate the mammalian NPFF receptor, under conditions permitting activation of the mammalian NPFF receptor;

30 (b) determining whether the activity of the mammalian NPFF receptor is increased in the presence of the compounds; and if so

(c) separately determining whether the activation of the mammalian NPFF receptor is increased by each compound included in the plurality of compounds, so as to thereby identify the compound which activates the mammalian NPFF receptor.

159. A method of claim 158, wherein the mammalian NPFF receptor is a human NPFF1 receptor.

160. A method of claim 158, wherein the mammalian NPFF receptor is a human NPFF2 receptor.

161. A method of screening a plurality of chemical compounds not known to inhibit the activation of a mammalian NPFF receptor to identify a compound which inhibits the activation of the mammalian NPFF receptor, which comprises:

(a) contacting cells transfected with and expressing the mammalian NPFF receptor with the plurality of compounds in the presence of a known mammalian NPFF receptor agonist, under conditions permitting activation of the mammalian NPFF receptor;

(b) determining whether the activation of the mammalian NPFF receptor is reduced in the presence of the plurality of compounds, relative to the activation of the mammalian NPFF receptor in the absence of the plurality of compounds; and if so

(c) separately determining the inhibition of

activation of the mammalian NPFF receptor for each compound included in the plurality of compounds, so as to thereby identify the compound which inhibits the activation of the mammalian NPFF receptor.

5

162. A method of claim 161, wherein the mammalian NPFF receptor is a human NPFF1 receptor.

10

163. A method of claim 161, wherein the mammalian NPFF receptor is a human NPFF2 receptor.

15

164. A method of any of claims 158, 159, 160, 161, 162, or 163, wherein the cell is a mammalian cell.

165. A method of claim 164, wherein the mammalian cell is non-neuronal in origin.

20

166. The method of claim 165, wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a LM(tk-) cell or an NIH-3T3 cell.

25

167. A pharmaceutical composition comprising a compound identified by the method of claim 158 or 159 effective to increase mammalian NPFF receptor activity and a pharmaceutically acceptable carrier.

30

168. A pharmaceutical composition comprising a compound identified by the method of claim 161 or 162 effective to decrease mammalian NPFF receptor activity and a pharmaceutically acceptable carrier.

169. A method of treating an abnormality in a subject wherein the abnormality is alleviated by increasing the activity of a mammalian NPFF receptor which comprises administering to the subject an amount of a compound which is a mammalian NPFF receptor agonist effective to treat the abnormality.
170. A method of claim 169, wherein the abnormality is a regulation of a steroid hormone disorder, an epinephrine release disorder, a gastrointestinal disorder, a cardiovascular disorder, an electrolyte balance disorder, hypertension, diabetes, a respiratory disorder, asthma, a reproductive function disorder, an immune disorder, an endocrine disorder, a musculoskeletal disorder, a neuroendocrine disorder, a cognitive disorder, a memory disorder, a sensory modulation and transmission disorder, a motor coordination disorder, a sensory integration disorder, a motor integration disorder, a dopaminergic function disorder, an appetite disorder, obesity, a sensory transmission disorder, an olfaction disorder, a sympathetic innervation disorder, pain, psychotic behavior, morphine tolerance, opiate addiction, affective disorder, or migraine.
171. A method of treating an abnormality in a subject wherein the abnormality is alleviated by decreasing the activity of a mammalian NPFF receptor which comprises administering to the subject an amount of a compound which is a mammalian NPFF receptor antagonist effective to

treat the abnormality.

172. A method of claim 171, wherein the abnormality is
a regulation of steroid hormone disorder, an
epinephrine release disorder, a gastrointestinal
disorder, a cardiovascular disorder, an
electrolyte balance disorder, hypertension,
diabetes, a respiratory disorder, asthma, a
reproductive function disorder, an immune
disorder, an endocrine disorder, a
musculoskeletal disorder, a neuroendocrine
disorder, a cognitive disorder, a memory
disorder, a sensory modulation and transmission
disorder, a motor coordination disorder, a
sensory integration disorder, a motor integration
disorder, a dopaminergic function disorder, an
appetite disorder, obesity, a sensory
transmission disorder, an olfaction disorder, a
sympathetic innervation disorder, pain, psychotic
behavior, morphine tolerance, opiate addiction,
affective disorder, or migraine.

173. A process for making a composition of matter
which specifically binds to a mammalian NPFF
receptor which comprises identifying a chemical
compound using the process of any of claims 76,
77, 97, 98, 107, or 108 and then synthesizing the
chemical compound or a novel structural and
functional analog or homolog thereof.

174. A process for making a composition of matter
which specifically binds to a mammalian NPFF
receptor which comprises identifying a chemical
compound using the process of any of claims 134,

142, or 158 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.

5. 175. A process for making a composition of matter which specifically binds to a mammalian NPFF receptor which comprises identifying a chemical compound using the process of any of claims 135, 144, 161 and then synthesizing the chemical
10 compound or a novel structural and functional analog or homolog thereof.

176. The process of any of claims 173, 174, or 175, wherein the mammalian NPFF receptor is a human
15 NPFF1 receptor.

177. The process of any of claims 173, 174, or 175, wherein the mammalian NPFF receptor is a human
20 NPFF2 receptor.

21 178. A process for preparing a pharmaceutical composition which comprises admixing a pharmaceutically acceptable carrier and a pharmaceutically acceptable amount of a chemical
25 compound identified by the process of any of claims 76, 77, 97, 98, 107, or 108 or a novel structural and functional analog or homolog thereof.

30 179. A process for preparing a pharmaceutical composition which comprises admixing a pharmaceutically acceptable carrier and a pharmaceutically acceptable amount of a chemical compound identified by the process of any of

158 or a
or homolo
preparin
n comp
acceptab
ceptable
d by th
161 or a
or homolo
of cla
ian NPFI
of cla
ian NPFI

- add A27
add C27

5

10.

15